

Novel process for the preparation of a synthetic intermediate for pesticides

5 The present invention relates to a novel process for the preparation of a
2,6-dihalo-para-trifluoromethylaniline from para-trifluoromethylaniline.

Numerous studies have already been carried out with the aim of developing
processes for the preparation of 2,6-dihalo-para-trifluoromethylanilines. Patent
Application WO 00/35851 discloses a process for the preparation of a 2,6-dihalo-
10 para-trifluoromethylaniline from a trihalo-para-trifluoromethylbenzene at a
temperature of between 130 and 350°C in a preferably polar solvent. The use of para-
trifluoromethylaniline for the preparation of 2,6-dihalo-para-trifluoromethylaniline
does not appear in this patent application.

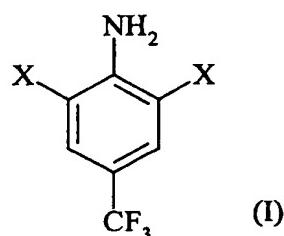
15 Patent Applications FR 2 810 665 and WO 01/64623 disclose a process for
the preparation of 2,6-dichloro-para-trifluoromethylaniline by chlorination of
precursor anilines in a hydrofluoric acid medium. The precursor compound is
trifluoromethylphenylcarbamoyl fluoride. The use of an other solvent than
hydrofluoric acid is not mentioned.

20 Nevertheless, these processes result in the formation of impurities, such as
polycondensates or heavy polychlorinated compounds, which make it impossible to
use 2,6-dihalo-para-trifluoromethylaniline in the continuation of the preparation of
pesticidal compounds of phenylpyrazole type without subjecting it to a prior
25 purification stage. This purification stage constitutes a major disadvantage when it is
a matter of preparing 2,6-dichloro-para-trifluoromethylaniline on an industrial scale,
in particular for the production of pesticides of phenylpyrazole type.

30 It has now been discovered, in an entirely surprising way, that the process for
the preparation of 2,6-dihalo-para-trifluoromethylaniline according to the present
invention results in a compound which is sufficiently pure to be used directly in the
continuation of the process for the production of pesticidal compounds of
phenylpyrazole type.

A subject-matter of the present invention is thus a process for the preparation of a compound of general formula (I):

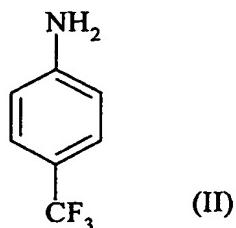
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in which X represents a halogen atom,
by reaction of para-trifluoromethylaniline of formula (II):

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with a dihalogen X₂,

the two compounds being introduced simultaneously into a polar aprotic solvent at a temperature ranging from 100 to 300°C and at a dihalogen/compound (II) molar ratio

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ranging from 1.9 to 2.5.

In the context of the present invention, X represents a halogen atom. X can be a chlorine atom, a bromine atom, an iodine atom or a fluorine atom.

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The compound of general formula (I) preferably prepared by virtue of the process according to the present invention is 2,6-dichloro-para-trifluoromethylaniline, which is particularly useful in the synthesis of fipronil, an insecticidal compound of phenylpyrazole type.

The solvent used during the preparation of the compound of general formula (I) according to the present invention is a polar aprotic solvent. A preferred polar aprotic solvent can be a chlorinated aromatic solvent, such as monochlorobenzene, or a chlorinated aliphatic solvent, such as dichloroethane. In an entirely preferred way, 5 monochlorobenzene will be chosen as solvent.

The dihalogen/compound (II) molar ratio is chosen as ranging from 1.9 to 2.5 during the preparation of the 2,6-dihalo-para-trifluoromethylaniline according to the 10 present invention. The dihalogen/compound (II) molar ratio is preferably chosen as ranging from 2 to 2.05.

The temperature of the reaction medium according to the present invention is chosen as ranging from 100 to 300°C. The temperature of the reaction medium is preferably chosen as ranging from 100 to 130°C. In an entirely preferred way, the 15 temperature of the reaction medium is chosen as ranging from 105°C to 115°C.

In an entirely preferred way, the process according to the present invention consists in preparing 2,6-dichloro-para-trifluoromethylaniline by simultaneously introducing para-trifluoromethylaniline and Cl₂ into monochlorobenzene in a 20 Cl₂/para-trifluoromethylaniline molar ratio of between 1.85 and 2.05, at a temperature ranging from 105 to 115°C.

The process according to the present invention can be carried out according to general techniques known to a person skilled in the art. Thus, the process according 25 to the present invention can be carried out in a jacketed reactor equipped with a stirring device and surmounted by a reflux condenser maintained at a temperature of less than or equal to -10°C. The halogen necessary for the reaction will be introduced via a dip pipe arriving with stirring. The stirrer preferably used will make it possible to provide optimum micromixing of the reactants. This can be carried out by a stirrer 30 of impeller type or by any other stirrer well known to a person skilled in the art.

During the reaction according to the present invention, hydrochloric acid in the gaseous form is produced. The latter is subsequently generally absorbed by a sodium hydroxide trap. As para-trifluoromethylaniline reacts instantaneously on 35 contact with hydrochloric acid to form para-trifluoromethylaniline hydrochloride,

para-trifluoromethylaniline will preferably be fed to the reactor via a dip pipe, in order to avoid blockages.

During the introduction of the reactants, a marked tendency to foam is sometimes observed. This can generally be avoided by reducing the flow rate for the introduction of the reactants. Nevertheless, in order to avoid the accumulation of foam, the latter should be taken up by the liquid. One answer is therefore generally to increase the stirring rate.

The product obtained by virtue of the process according to the present invention (2,6-dihalo-para-trifluoromethylaniline) has a sufficient degree of purity to be reused directly in the synthesis of the pesticidal compounds of phenylpyrazole type. It is generally considered that the degree of purity should be at least 96% in order for the product to be able to be used in the continuation of a preparation process.

The 2,6-dihalo-para-trifluoromethylaniline obtained can also be isolated, in particular in order to be stored, by distillation of the solvent according to techniques known to a person skilled in the art.

The example of the preparation of compounds which follows is mentioned with the aim of illustrating the invention but should on no account be regarded as limiting the latter.

25 Preparation of 98% 2,6-dichloro-para-trifluoromethylaniline

12 140 kg of pure monochlorobenzene are charged to a 20 m³ jacketed reactor rendered inert with nitrogen. The solvent heel is subsequently brought to 110°C by heating the jacket.

The reactor is subsequently fed with a 70% solution of para-trifluoromethylaniline in monochlorobenzene at a flow rate of 792 kg/h for 6 h 30 and with Cl₂ at a flow rate of 488 kg/h. The temperature is maintained at 110°C by cooling the jacket.

Once feeding is complete, the residual content of para-trifluoromethylaniline or of monochloro derivative is monitored. If one of these compounds remains, it is then advisable to adjust the amount of chlorine in order to consume the residual product.

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At the end of the reaction, the monochlorobenzene is distilled off by placing the reactor under gradually increasing vacuum through a distillation column. After removal of the solvent, the 2,6-dichloro-para-trifluoromethylaniline is cooled to 60°C before emptying the reactor to the storage tank.

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The product obtained according to the process described above was analysed. The results given in the table below correspond to the mean of the analytical results which are obtained for the product over a period of one year:

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DCpTFMA assay (solvent-free)	p-TFMA assay (solvent-free)	Monochloro-para- trifluoromethylaniline assay
98.1%	0.05%	0.09%

These results thus show that the 2,6-dichloro-para-trifluoromethylaniline obtained by the process according to the present invention is pure to greater than 98%, that the reaction yield is very good, since only 0.05% of reactant (p-TFMA)

20 remains, and that only 0.09% of the monochloro-para-trifluoromethylaniline has not been converted to 2,6-dichloro-para-trifluoromethylaniline.